

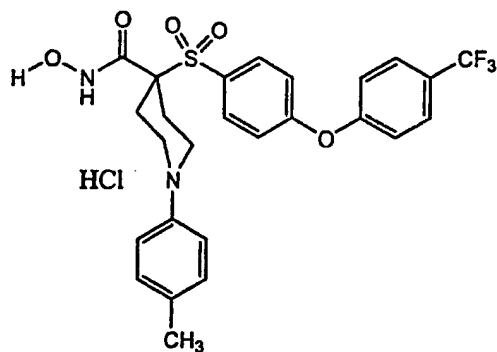
What is claimed is:

1. A method for treating neoplasia in a mammal in need of such treatment, comprising treating said mammal with radiation therapy and a therapeutically effective amount of a matrix metalloproteinase inhibitor or pharmaceutically-acceptable salt thereof.

2. The method of Claim 1 wherein the neoplasia is selected from the group consisting of lung cancer, breast cancer, gastrointestinal cancer, bladder cancer, head and neck cancer and cervical cancer.

3. A method for treating neoplasia in a subject in need of such treatment, comprising treating said mammal with radiation therapy and a therapeutically effective amount of a matrix metalloproteinase inhibitor or pharmaceutically-acceptable salt thereof, wherein the matrix metalloproteinase inhibitor is selected from compounds, and their pharmaceutically acceptable salts thereof, of the group consisting of

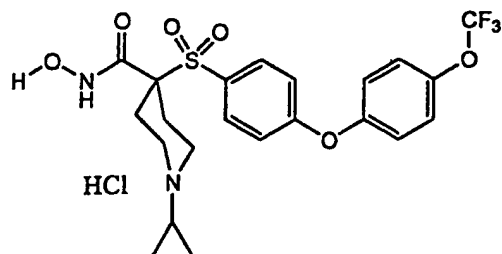
1) 20



N-hydroxy-1-(4-methylphenyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride;

104

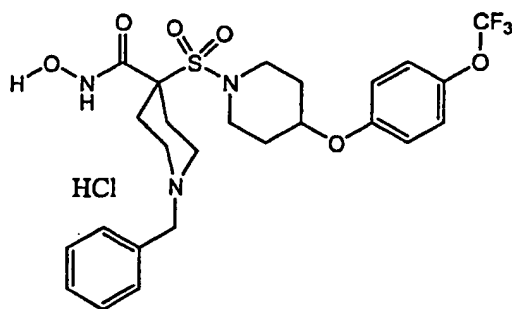
2)



5

1-cyclopropyl-N-hydroxy-4-[[4-[4-(trifluoromethoxy)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride;

3)

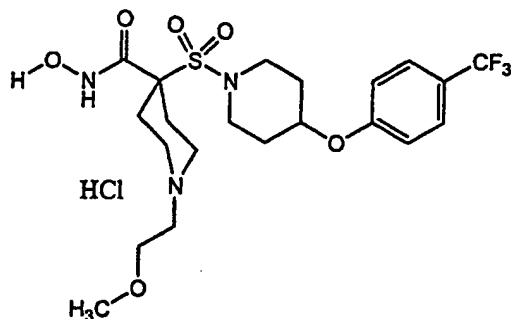


10

N-hydroxy-1-(phenylmethyl)-4-[[4-[4-(trifluoromethoxy)phenoxy]-1-piperidinyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride;

105

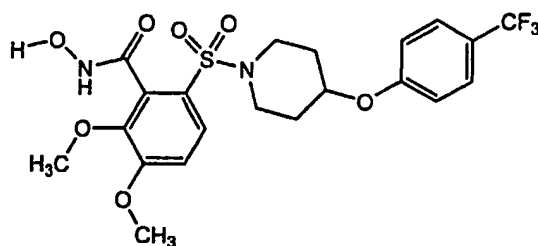
4)



N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride;

5

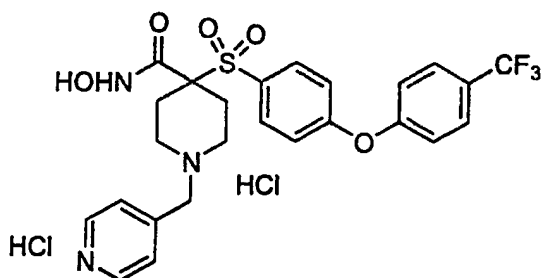
5)



N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide;

10

6)

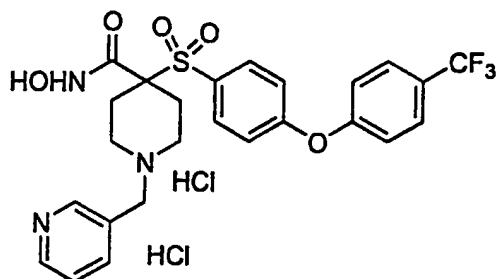


N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride;

15

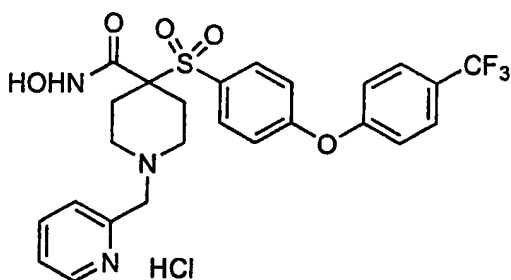
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7)



N-hydroxy-1-(3-pyridinylmethyl)-4-[[4-[(4-(trifluoromethyl)phenoxy]phenyl)sulfonyl]-4-piperidinecarboxamide dihydrochloride;

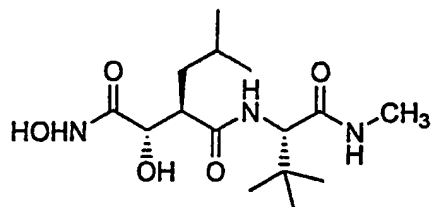
8)



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N-hydroxy-1-(2-pyridinylmethyl)-4-[[4-[(4-(trifluoromethyl)phenoxy]phenyl)sulfonyl]-4-piperidinecarboxamide monohydrochloride;

9)

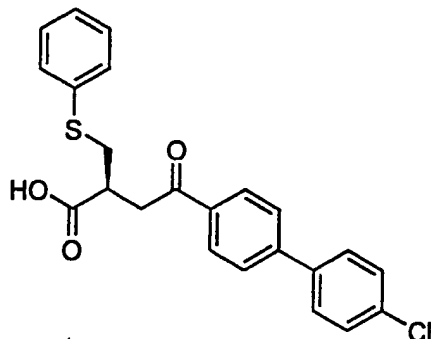


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British Biotech BB-2516 (Marimastat), N4-[2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-N1,2-dihydroxy-3-(2-methylpropyl)-, [2S-[N4(R*),2R*,3S*]]-;

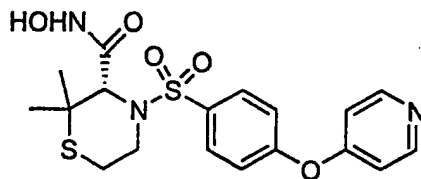
107

10)



Bayer Ag Bay-12-9566, 4-[(4'-chloro[1,1'-
iphenyl]- 4-yl)oxy]-2-
5 [(phenylthio)methyl]butanoic acid;

11)



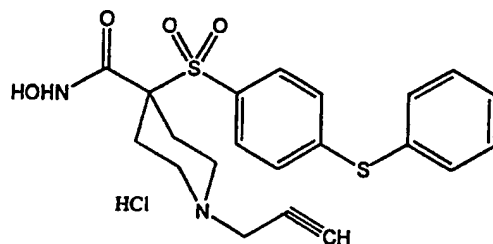
Agouron Pharmaceuticals AG-3340, N-hydroxy-
10 2,2- dimethyl- 4-[[4-(4-
pyridinyloxy)phenyl]sulfonyl]- 3-
thiomorpholinecarboxamide;

12) CollaGenex Pharmaceuticals CMT-3 (Metastat),
15 6- demethyl-6-deoxy-4-
dedimethylaminotetracycline;

13) Chiroscience D-2163, 2- [1S- ((2R,S)-
20 acetylmercapto- 5- phthalimido]pentanoyl- L-
leucyl)amino- 3- methylbutyl]imidazole;

108

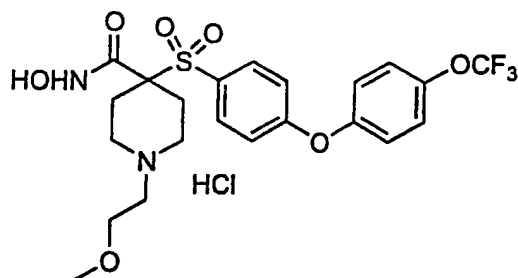
14)



N-hydroxy-4-[[4-(phenylthio)phenyl]sulfonyl]-
1-(2-propynyl)-4-piperidinecarboxamide
monohydrochloride;

5

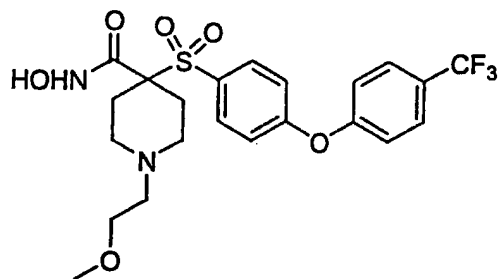
15)



N-hydroxy-1-(2-methoxyethyl)-4-[[4-[4-
(trifluoromethoxy) phenoxy]phenyl]sulfonyl]-4-
piperidinecarboxamide monohydrochloride;

10

16)

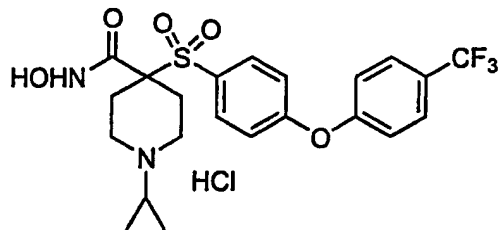


N-hydroxy-1-(2-methoxyethyl)-4-[[4-[4-
(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-
piperidinecarboxamide;

15

108
14)
15)
16)
15

17)



5

CC#CCN1CCCCC1C(=O)N.O=S(=O)(c2ccc(SC3CCCCC3)cc2)C1

10

O=C(O)C1(C(=O)S(=O)(=O)c2ccc(Oc3ccc(Cl)cc3)cc2)OCCO1

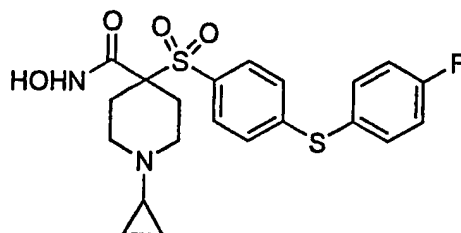
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COc1ccc(Oc2ccc(S(=O)(=O)C3(CCCC3C(=O)O)CN3CC#C)cc2)cc1

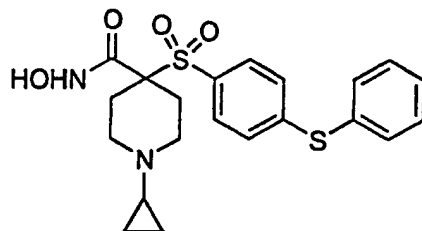
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21)



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22)

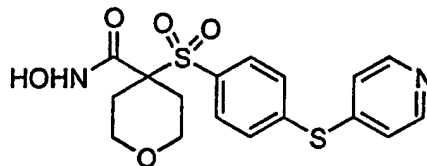


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[illegible]

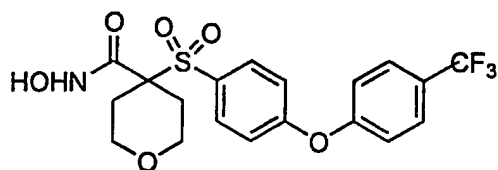
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23)



tetrahydro-N-hydroxy-4-[[4-(4-
pyridinylthio)phenyl]sulfonyl]-2H-pyran-4-
carboxamide;

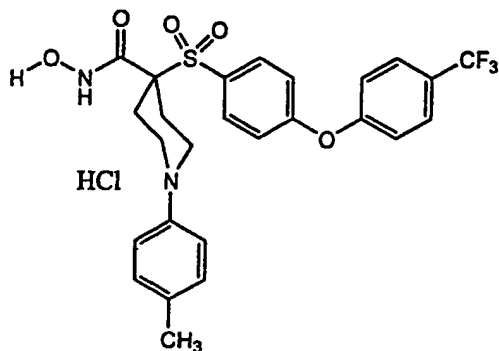
24)



tetrahydro-N-hydroxy-4-[[4-[4-
(trifluoromethyl)phenoxy]phenyl]sulfonyl]-2H-
pyran-4-carboxamide.

4. A method for treating neoplasia in a mammal
in need of such treatment, comprising treating said
mammal with radiation therapy and a therapeutically
effective amount of a matrix metalloproteinase
inhibitor or pharmaceutically-acceptable salt
thereof, wherein the matrix metalloproteinase
inhibitor is selected from compounds, and their
pharmaceutically acceptable salts thereof, of the
group consisting of

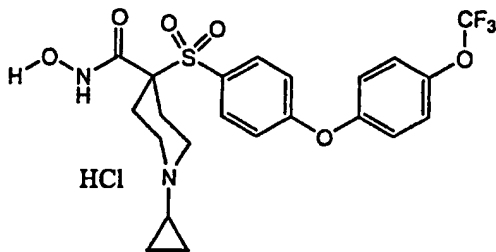
1)



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N-hydroxy-1-(4-methylphenyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride;

2)

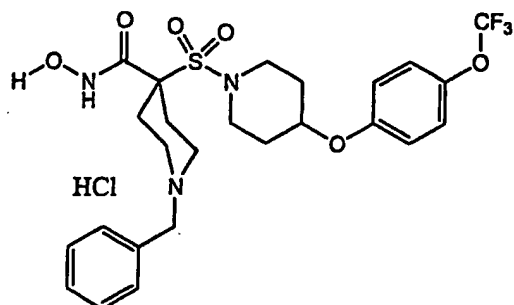


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1-cyclopropyl-N-hydroxy-4-[[4-[4-(trifluoromethoxy)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride;

113

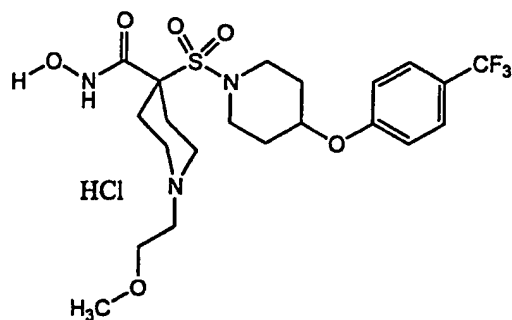
3)



N-hydroxy-1-(phenylmethyl)-4-[[4-[4-(trifluoromethoxy)phenoxy]-1-piperidinyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride;

5

4)

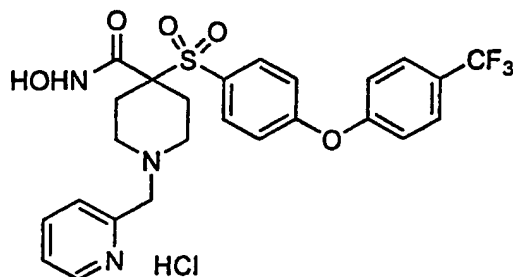


N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride;

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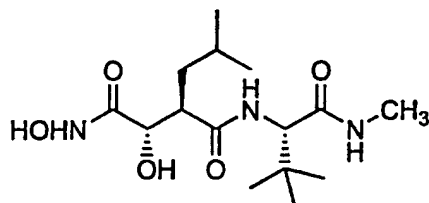
[illegible]

8)



N-hydroxy-1-(2-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride;

9)

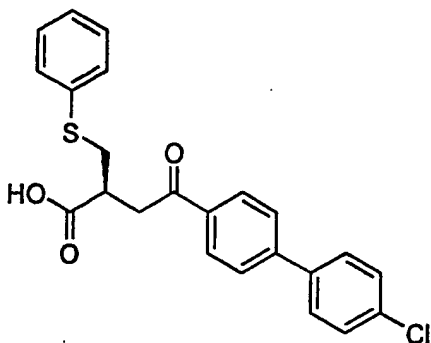


British Biotech BB-2516 (Marimastat), N4-[2,2-dimethyl- 1-[(methylamino)carbonyl]propyl]- N1,2 -dihydroxy-3 (2-methylpropyl)-, [2S-[N4(R*), 2R*, 3S*]]-);

15

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10)

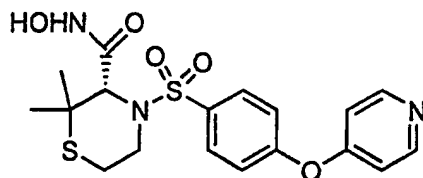


Bayer Ag Bay-12-9566, 4-[(4'-chloro[1,1'-
iphenyl]- 4-yl)oxy]-2-

5

[(phenylthio)methyl]butanoic acid;

11)



Agouron Pharmaceuticals AG-3340, N-hydroxy-

10

2,2- dimethyl- 4-[[4-(4-
pyridinyloxy)phenyl]sulfonyl]- 3-
thiomorpholinecarboxamide;

12) CollaGenex Pharmaceuticals CMT-3 (Metastat),

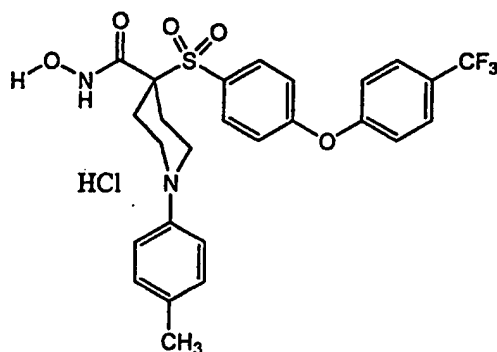
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6-demethyl-6-deoxy-4-
dedimethylaminotetracycline; and

13) Chiroscience D-2163, 2- [1S- ([(2R,S)-
acetylmercapto- 5- phthalimido]pentanoyl- L-
leucyl)amino- 3- methylbutyl]imidazole.

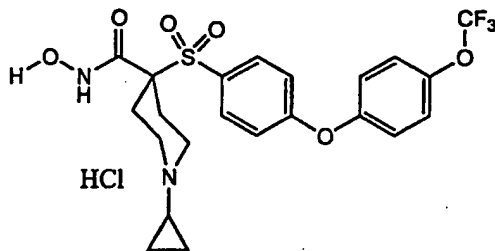
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5. The method of claim 3 wherein the matrix metalloproteinase inhibitor is

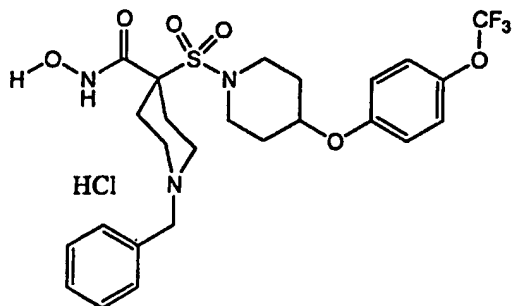


N-hydroxy-1-(4-methylphenyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

6. The method of claim 3 wherein the matrix metalloproteinase inhibitor is

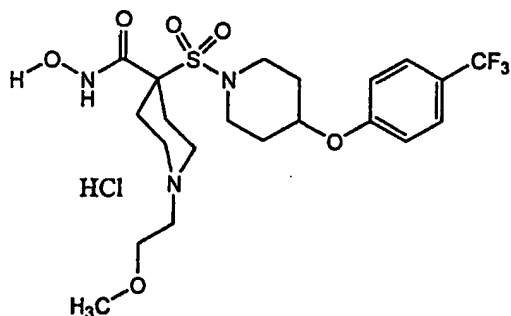


1-cyclopropyl-N-hydroxy-4-[[4-[4-(trifluoromethoxy)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.



5 N-hydroxy-1-(phenylmethyl)-4-[[4-[4-(trifluoromethoxy)phenoxy]-1-piperidinyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

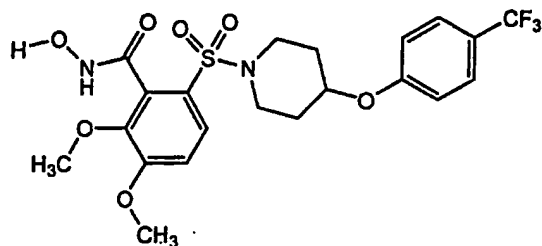
10 8. The method of claim 3 wherein the matrix metalloproteinase inhibitor is



15 N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride.

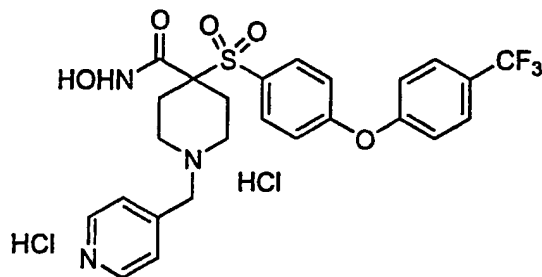
[illegible]

9. The method of claim 3 wherein the matrix metalloproteinase inhibitor is



5 N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide.

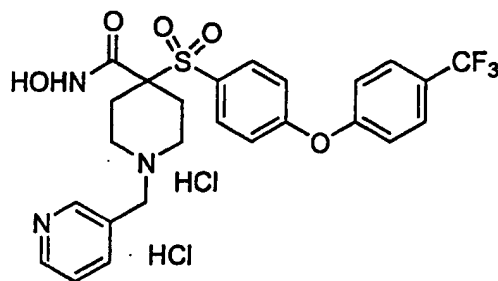
10. The method of claim 3 wherein the matrix
10 metalloproteinase inhibitor is



15 N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride.

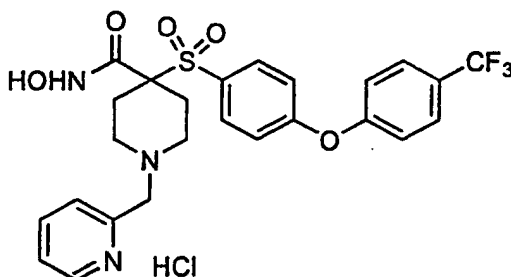
120

11. The method of claim 3 wherein the matrix metalloproteinase inhibitor is



5 N-hydroxy-1-(3-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride.

12. The method of claim 3 wherein the matrix
10 metalloproteinase inhibitor is

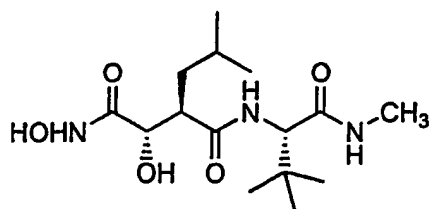


15 N-hydroxy-1-(2-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

13. The method of claim 3 wherein the matrix metalloproteinase inhibitor is

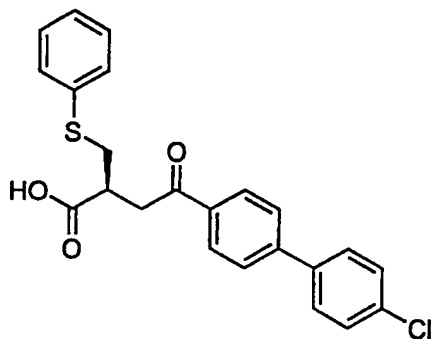
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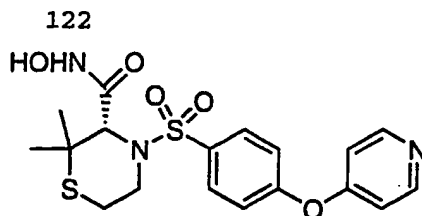
British Biotech BB-2516 (Marimastat), N4-[2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-N1,2-dihydroxy-3-(2-methylpropyl)-, [2S-[N4(R*),2R*,3S*]]-).

14. The method of claim 3 wherein the matrix metalloproteinase inhibitor is



15. Bayer Ag Bay-12-9566, 4-[(4'-chloro[1,1'-iphenyl]-4-yl)oxy]-2-[(phenylthio)methyl]butanoic acid.

15. The method of claim 3 wherein the matrix metalloproteinase inhibitor is



Agouron Pharmaceuticals AG-3340, N-hydroxy-
2,2- dimethyl- 4-[[4-(4-
pyridinyloxy)phenyl]sulfonyl]- 3-
thiomorpholinecarboxamide.

16. The method of claim 3 wherein the matrix
metalloproteinase inhibitor is CollaGenex
Pharmaceuticals CMT-3 (Metastat), 6-demethyl-6-deoxy-4-
dedimethylaminotetracycline.

17. The method of claim 3 wherein the matrix
metalloproteinase inhibitor is Chiroscience D-2163, 2-
[1S- ((2R,S)- acetylmercapto- 5- phthalimido]pentanoyl-
L- leucyl)amino- 3- methylbutyl]imidazole.

18. A combination comprising radiation therapy and
a therapeutically effective amount of a matrix
metalloproteinase inhibitor or pharmaceutically-
acceptable salt thereof.

19. The method of Claim 1 wherein the combination
is administered in a sequential manner.

20. The method of Claim 1 wherein the combination
is administered in a substantially simultaneous manner.

21. The method of Claim 3 wherein the combination
is administered in a sequential manner.

PCT/US99/30676